2013-01-01

The distribution of quick phase interval durations in human optokinetic nystagmus.

Waddington, J

<http://hdl.handle.net/10026.1/8352>

10.1007/s00221-012-3297-z

Exp Brain Res

Springer Science and Business Media LLC

All content in PEARL is protected by copyright law. Author manuscripts are made available in accordance with publisher policies. Please cite only the published version using the details provided on the item record or document. In the absence of an open licence (e.g. Creative Commons), permissions for further reuse of content should be sought from the publisher or author.

The distribution of quick phase interval durations in human optokinetic nystagmus

Jonathan Waddington & Christopher M. Harris

Experimental Brain Research

ISSN 0014-4819

Exp Brain Res
DOI 10.1007/s00221-012-3297-z

Your article is protected by copyright and all rights are held exclusively by Springer-Verlag Berlin Heidelberg. This e-offprint is for personal use only and shall not be self-archived in electronic repositories. If you wish to self-archive your work, please use the accepted author's version for posting to your own website or your institution's repository. You may further deposit the accepted author's version on a funder's repository at a funder's request, provided it is not made publicly available until 12 months after publication.

The distribution of quick phase interval durations in human optokinetic nystagmus

Jonathan Waddington · Christopher M. Harris

Received: 19 June 2012 / Accepted: 3 October 2012
© Springer-Verlag Berlin Heidelberg 2012

Abstract There is an interesting dichotomy between models that predict the quick phase interval durations (QPIDs) of human optokinetic nystagmus (OKN). Accumulator models describe a stochastic signal in a neural network that triggers a response once the signal reaches a fixed threshold value. However, it is also possible that quick phases are triggered after eye position reaches a variable amplitude threshold. In this study, we fitted a range of probability density functions previously predicted by stochastic models of OKN (including those of the reciprocal truncated Normal, inverse Gaussian, gamma, lognormal and the mixture of two reciprocal truncated Normal distributions) to individual QPID histograms. We compared the goodness of fit between these models, and a model where the distribution of QPIDs is determined by the ratio of two correlated and truncated Normal random variables. The ratio distribution gave the best fit to the data, and we propose this is due to the approximately linear trajectory of slow phases (SPs) and that QPIDs are given by the ratio of a variable SP amplitude threshold and variable SP velocity.

Keywords Optokinetic nystagmus · Quick phase interval · Ratio distribution · Accumulator models · Distribution analysis · Variable threshold

Abbreviations

OKN Optokinetic nystagmus
SP Slow phase
QP Quick phase

QPID Quick phase interval duration
pdf Probability density function
MLE Maximum likelihood estimate
dof Degrees of freedom

Introduction

Optokinetic nystagmus (OKN) is a gaze-stabilising response that is essential for maintaining vision during prolonged head and body movements. Compensatory eye movements are elicited in response to the optic flow generated by locomotion, and they are characterised by an alternating sequence of compensatory slow phases (SPs) in the direction of optic flow, and quick phases (QPs) which are usually made in the opposite direction. The amplitude and timing of QPs and SPs are remarkably variable, and while there is general agreement on the mechanism that generates SPs, the mechanisms that generate QPs are not well understood.

The QP trigger is commonly modelled as a stochastic interval generator that is accumulating evidence to a constant threshold value when a decision is made to generate a QP. The stochastic nature of the signal (inspired by the behaviour of firing neurons) gives rise to the variability in duration. Carpenter (1993) suggested that quick phase interval durations (QPIDs) could be described with a reciprocal Normal distribution (rectrRN) based on his LATER (linear rise to threshold with ergodic rate) model, in which a decision signal accumulates linearly in time with a rate that varies between QPs with a Normal distribution. The modern LATER model (Carpenter and Williams 1995) hypothesises that there are actually two LATER decision signals competing in a race to threshold,

J. Waddington (✉) · C. M. Harris
Plymouth Cognition Institute & Centre for Robotics and Neural Systems, Plymouth University, Plymouth, Devon PL4 8AA, UK
e-mail: jonathan.waddington@plymouth.ac.uk

which would generate QPIDs with a mixture of two reciprocal Normal distributions (mixRN). This model predicts that QPs are triggered when one of the accumulators reaches its threshold first, at which point both signals are reset and the competition begins again. Notably, one of the signals is usually considered to be unbiased (i.e. it has zero mean rate) but varies with a much larger standard deviation than the other, occasionally generating extremely short latency QPs (Carpenter 1994).

Anastasio (1996) suggested that QPIDs could be described with the inverse Gaussian distribution (IG), based on a model describing the integration of noisy vestibular nucleus neurons as a random walk with drift towards a threshold (diffusion process). A similar integrate-to-fire model, where individual spikes occur at exponentially distributed time intervals until an integer threshold of spikes have been reached, produces the gamma distribution (GAM) (Tuckwell 1988). Finally, Balaban and Ariel (1991) have also suggested that QPIDs could be described with the lognormal distribution (LN).

Trillenberget al. (2002) performed a comprehensive comparison of seven probability density functions (pdfs), including the reciprocal Normal, inverse Gaussian, gamma and lognormal distributions. However, none of the distributions tested were able to fit the data especially well, and it was concluded that a large amount of data were required to determine significant differences in the goodness of fit of each distribution.

The implication of all these accumulator models is that QPs are triggered by a time interval generator, and that SP amplitude is determined by the product of SP velocity and SP duration due to the linear trajectory of SPs:

$$TV \Rightarrow A \quad (1)$$

However, another possibility is that the QP trigger is based on a variable position or amplitude threshold, and variability in QPIDs is instead determined by the variability in SP amplitude and/or SP velocity:

$$\frac{A}{V} \Rightarrow T \quad (2)$$

Recently, Harris and Waddington (2012) illustrated a case of OKN where the distribution of QPIDs and reciprocal QPIDs (QP rate) were both highly skewed, such that the moments (mean, standard deviation, kurtosis, etc.) of the parent distributions did not appear to converge to finite values. The mean of a distribution will not converge to a finite value if the pdf of the reciprocal distribution has a nonzero probability of being zero, and higher moments will also fail to converge depending on the behaviour of the reciprocal pdf near zero. We note that the reciprocal pdf of a ratio of two unbounded distributions is also a ratio of two unbounded distributions, and that both ratio distributions would be

highly skewed and would not have finite moments. We, therefore, hypothesise that the QPID distribution may be a ratio distribution, parsimoniously determined by the ratio of a variable SP amplitude threshold and variable SP velocity.

As Trillenberget al. pointed out, it is necessary to collect large amounts of data to determine significant differences between similar statistical models. In this investigation, we recorded OKN eye movements over long periods to collect hundreds of QPIDs over each trial, and thousands when datasets were combined. We fitted 6 different models to 40 datasets individually, with maximum likelihood estimates (MLEs) of the parameters from their predicted pdfs, and compared the goodness of fit of these pdfs with each other. We found that the pdf describing the ratio of two correlated and zero-truncated Normal variables gave the best fit to the data. We propose that the QPID is determined by the ratio of a variable amplitude threshold and a variable SP velocity that changes from SP to SP.

Materials and methods

Participants

Ten healthy adults (6 females and 4 males), mean age 25 (SD = 5) years, participated in the study and had no neurological, ophthalmological or vestibular impairments. All protocols were approved by Plymouth University Faculty of Science Human Research Ethics Committee, and participants gave informed consent and were made aware of their right to withdraw at any time.

Procedure

Participants sat in a chair 1 m from the middle of a flat white screen, subtending 76° by 61°, and the OKN stimulus was rear projected (EPSON EMP-500; Seiko Epson Corp., Japan) onto the screen. Eye movements were measured using a binocular head-mounted limbus tracker (Skalar IRIS Infrared Light Eye Tracker; Skalar Medical BV, Netherlands) that recorded horizontal movement with a resolution of 3 minarc at a sampling rate of 1 kHz. The participant's head was constrained with a chin rest. Eye movement measurements were recorded on computer (vsgEyetrace v.3.0.beta software for Windows; Cambridge Research Systems, UK) and stored for offline analysis.

Stimulus

Translational OKN was elicited with a flat vertical square wave gratings comprised of alternating black and white stripes (0.1 cycles/°). Recording sessions were composed of a pseudorandom sequence of 4 experimental trials, each

with a different stimulus speed (10°/s, 20°/s, 30°/s or 40°/s) for a period of 160 s. Participants were asked to stare at the centre of the screen rather than follow the moving lines, to evoke 'stare' OKN rather than 'look' OKN, and attention to the stimulus was maintained by giving brief verbal feedback approximately every 10 s during stimulation. Participants were given a break for 1 min between each trial to alleviate discomfort, tiredness and to minimise the effects of any optokinetic after-nystagmus.

Data analysis

Movement in the direction of the stimulus motion was defined as positive, and movement in the opposite direction as negative. Position (relative to the centre) on the side that the stimulus is moving towards was defined as positive and the opposite side as negative. All programs and algorithms for analysing data were developed and created in MATLAB (MATLAB; Mathworks, USA). Each eye was calibrated separately, and the average 'cyclopean' eye position was computed. Eye velocity was derived from the cyclopean eye position using a central difference algorithm and zero-phase digital filtered with an 80 Hz Butterworth filter. Eye acceleration was derived from the filtered eye velocity data using a central difference algorithm.

Possible QPs were detected when eye acceleration reached a magnitude greater than 1,000°/s². Eye velocity was then recorded during a forward pass of the data, and the peak velocity was determined at the time when velocity first began to decrease in magnitude and further remained at a lower magnitude for 4 ms. The start and end of each QP were then determined by a respective backward and forward pass of the data from the time of peak velocity to the time when eye velocity returned to a value between 0°/s and stimulus speed for 2 ms. In this way, we were able to collect QPs that were made in the direction of optic flow as well as QPs made in the opposite direction. All eye movements were reviewed and verified in a customised interactive graphical interface. Blinks were detected manually and intervals containing blinks were marked and removed before analysis. The first 10 s of eye movement recordings was also removed before analysis to ignore 'early' (transitional) OKN behaviour.

After blinks and 'early' OKN behaviour were extracted, each recorded trial contained m QP intervals, where m ranged from 69 to 471 (total = 10,280). We measured the QPID and the SP amplitude during each QP interval and calculated the SP velocity for each QP interval from the slope of linear regression performed on the position data across each interval. Repeated measures ANOVA was performed on mean SP velocity and amplitude to test for stimulus effects. As the distribution of QPIDs was usually

skewed with a heavy positive tail, the Friedman's two-way ANOVA by ranks was employed as a nonparametric test for stimulus effects.

Distribution fitting

We considered the goodness of fit of six different distributions to the QPID histogram from each trial: the ratio of two correlated and left truncated (at zero) Normal variables (RATIO($t; \mu, \sigma, \alpha, \rho$)), the reciprocal zero-truncated Normal (rectrN($t; \mu, \sigma^2$)), a mixture distribution of two reciprocal zero-truncated Normal variables with one mean fixed at zero (mixRN($t; p, \mu_1, \sigma_1^2, \sigma_0^2$), where $1 - p$ is the proportion of QPs generated by the unbiased accumulator), the inverse Gaussian (IG($t; \mu, \lambda$)), gamma (GAM($t; a, b$)) and lognormal (LN($t; \mu, \sigma$)). The proposed models that give rise to these distributions are illustrated in Fig. 1, and the pdfs and abbreviated notations of these distributions can be found in Table 1. As far as we are aware, the ratio of two correlated and zero-truncated Normal variables has not been investigated before in the literature, so we have included a derivation in the "Appendix".

We obtained MLEs of the pdf parameters using the MATLAB statistics toolbox function: *mle*. This routine searches for the parameters that maximise the log likelihood of a user-defined pdf, using a simplex algorithm. MLEs of correlation coefficients could not be reliably retrieved using this method as the likelihood function became irregular (not smooth) when the correlation coefficient was included in the simplex search, so we estimated the correlation coefficients using the sample Pearson's correlation coefficient between SP amplitude and SP velocity from each trial.

After finding the MLEs of the pdf parameters for each trial, we tested the goodness of fit of the pdf to the histogram using the χ^2 criterion: $\chi^2 = \sum (O_i - E_i)^2 / E_i$, where O_i is the observed frequency for bin i , E_i is the expected frequency for bin i , and summation occurs over all bins in one histogram. The test statistic was calculated using the MATLAB function: *chi2gof*, and the expected frequency was calculated from the fitted pdf at the midpoint of each bin. This test can be sensitive to the choice of bin sizes, so we used those chosen in a similar investigation (Trillenberg et al. 2002), where each QPID histogram was covered by 40 bins of equal size. The test performs poorly if the expected frequency in any given bin is small, so the *chi2gof* function automatically combines bins in the tails of each distribution until there is a minimum expected frequency of 5 in each bin.

The test statistic follows the χ^2 distribution with $v = N - n - 1$ degrees of freedom (dof), where N is the number of nonempty bins in the histogram, and n is the number of parameters estimated in the pdf. The null

Fig. 1 Models predicting the PDF of QPIDs as the result of either **a** the ratio of a variable amplitude or position threshold and variable slow phase velocity from SP to SP, or **b–d** a decision signal that triggers a QP after a threshold of accumulated evidence has been reached. A variable amplitude threshold may be generated by saccadic error in the QPs causing a variable position at the start of each SP. The models illustrated in **b–d** vary in the stochastic nature of how the decision signal rises to threshold. In **b**, the decision signal rises at a linear rate but the rate of rise varies from QP to QP with a Gaussian distribution, predicting a reciprocal Normal (rectrN)

distribution of QPIDs. In **c**, a noisy signal is integrated by a network of neurons over the period of each SP, generating a decision signal that rises in the same manner as Brownian motion with a constant drift rate (the diffusion process) and predicting an inverse Gaussian (IG) distribution of QPIDs. In **d**, an integer number of neuronal spikes are integrated over the period of each SP and a QP is generated after a certain number of spikes have been received (6, in this example). If the spikes are generated at a constant probability per unit time, this process predicts a Gamma (GAM) distribution of QPIDs

Table 1 Probability density functions investigated in this study

Distribution	Notation	pdf
Ratio of two correlated and zero-truncated Normal variables	$\text{RATIO}(t; \mu, \sigma, \alpha, \rho)$	See ‘Appendix’ for derivation (eq. 16)
Reciprocal zero-truncated Normal	$\text{rectrN}(t; \mu, \sigma^2)$	$\frac{\exp\left(-\frac{(1-\mu)^2}{2\sigma^2}\right)}{(1-\Phi(-\mu/\sigma))t^2\sqrt{2\pi\sigma^2}}$ <p>where $\Phi(\cdot)$ = Normal cdf</p>
Mixture of two reciprocal zero-truncated Normal variables, with one mean fixed at zero	$\text{mixrN}(t; p, \mu_1, \sigma_1^2, \sigma_0^2)$	$p\left(\frac{\exp\left(-\frac{(1-\mu_1)^2}{2\sigma_1^2}\right)}{(1-\Phi(-\mu_1/\sigma_1))t^2\sqrt{2\pi\sigma_1^2}}\right) + (1-p)\left(\frac{\exp\left(-\frac{1}{2\sigma_0^2}\right)}{0.5t^2\sqrt{2\pi\sigma_0^2}}\right)$ <p>where $1 - p$ = proportion of QPs generated by the unbiased accumulator</p>
Inverse Gaussian	$\text{IG}(t; \mu, \lambda)$	$\sqrt{\frac{\lambda}{2\pi t^3}} \exp\left(-\frac{\lambda(t-\mu)^2}{2\mu^2 t}\right)$
Gamma	$\text{GAM}(t; a, b)$	$\frac{t^{a-1}}{b^a \Gamma(a)} \exp\left(-\frac{t}{b}\right)$ <p>where $\Gamma(\cdot)$ = Gamma function</p>
Lognormal	$\text{LN}(t; \mu, \sigma)$	$\frac{\exp\left(-\frac{(\ln t - \mu)^2}{2\sigma^2}\right)}{t\sigma\sqrt{2\pi}}$

hypothesis that the data are from the tested distribution must be rejected if $\chi^2 > \chi^2_{\alpha, v}$, where $\chi^2_{\alpha, v}$ is the χ^2 inverse cumulative density function, and α is the level of significance ($\alpha = 0.05$). If the total dof were reduced to zero, we

conservatively assumed that the pdf being tested was significantly different to the observed histogram. Testing the null hypothesis for multiple comparisons was corrected using the Holm–Bonferroni method (Holm 1979).

The results of fitting one histogram with two different pdfs were compared by taking the ratio of the two test statistics scaled by their dof $F = (\chi_1^2/v_1)/(\chi_2^2/v_2)$ follows the F distribution with v_1, v_2 dof, where χ_1^2 and χ_2^2 are the test statistics derived from fitting two different pdfs to a single histogram, and v_1 and v_2 are the respective dof. Significant differences in the goodness of fit between two pdfs were revealed by a significant deviation of the value F from 1. Similarly, we compared the cumulative results of fitting all histograms with two different pdfs by summing the values of χ_1^2, χ_2^2, v_1 and v_2 over all histograms, such that $F = (\sum \chi_1^2 / \sum v_1) / (\sum \chi_2^2 / \sum v_2)$ follows the F distribution.

Repeated measures ANOVA was performed on goodness of fit test statistics and the MLEs of pdf parameters to test for stimulus speed effects.

Results

The data appeared typical of previously reported OKN responses. Increasing stimulus speed resulted in a decrease in the median QPID ($p = 0.006$), an increase in mean SP velocity ($p = 0.001$) and an increase in mean SP amplitude ($p < 0.001$) (Fig. 2). We did not observe any SPs made in the direction opposite stimulus motion, although 4 % of QPs were made in the direction of stimulus motion.

In 36 of 40 trials, the SP amplitude and SP velocity were significantly correlated (Holm–Bonferroni corrected t test; $p \leq 0.0016$) with a mean Pearson's correlation coefficient $r = 0.33$ (SD = 0.19) across all trials. In 32 of 40 trials, the QPID and SP velocity were also significantly correlated (Holm–Bonferroni corrected t test; $p \leq 0.0071$) with a mean Pearson's correlation coefficient $r = -0.31$ (SD = 0.22) across all trials. QPID and SP amplitude were significantly correlated in all trials (Holm–Bonferroni corrected t test; $p \leq 5.4 \times 10^{-6}$) with a mean Pearson's correlation coefficient $r = 0.67$ (SD = 0.24) indicating that SPs had linear trajectories. Finally, the start and end position of SPs were significantly correlated in all trials (Holm–Bonferroni corrected t test; $p \leq 8.9 \times 10^{-6}$) with a mean Pearson's correlation coefficient $r = 0.72$ (SD = 0.13), indicating that SP amplitude remained relatively constant during each trial. SP amplitude variance was significantly less than SP end position variance in 29 of 40 trials (Holm–Bonferroni corrected F test; $p \leq 0.0010$). The high correlation between SP start and end position, and correspondingly lower variability in SP amplitude, indicated that SP amplitude was under a higher degree of control than the end position of SPs within the positional range from which we recorded.

Fig. 2 Boxplots illustrating the effect of stimulus speed on **a** median QPID, **b** mean SP velocity and **c** mean SP amplitude. Each box represents the OKN variable grouped across all 10 participants for each stimulus condition: height of box interquartile range; whiskers minimum to maximum data values excluding outliers; filled circles outliers found more than $\times 1.5$ the interquartile range from the ends of the box. Asterisk notes significant differences in the dependent variable between stimulus conditions ($\alpha = 0.05$)

Histograms of QPIDs were usually positively skewed (Fig. 3a), and 34 of 40 trials generated histograms significantly different to Normal (Holm–Bonferroni corrected Lilliefors test; $p \leq 0.0053$). Histograms of instantaneous QP rate (1/QPID) were also usually positively skewed (Fig. 3b), and 37 of 40 trials generated histograms significantly different to Normal (Holm–Bonferroni corrected Lilliefors test; $p \leq 0.0023$).

Testing the goodness of fit of pdfs to individual histograms revealed three distinct groups, one that gave a good fit to 90 % of QPID histograms (RATIO), one that gave a good fit to 58–70 % of QPID histograms (mixRN, LN, IG, GAM), and one that gave a good fit to only 25 % of QPID histograms (rectrN) (Table 2). Note that the goodness of fit

Fig. 3 Representative frequency histograms of **a** QPIDs and **b** reciprocal QPIDs, from one trial. Data generated from participant 2 (stimulus condition: 20°/s)

test statistic takes into account the number of free parameters to be estimated for each pdf (see “Materials and methods”). After correcting for multiple comparisons, there was no significant main effect of stimulus speed on the goodness of fit test statistics for RATIO ($p = 0.68$), mixRN ($p = 0.36$), rectrN ($p = 0.085$), LN ($p = 0.079$), IG ($p = 0.031$) or GAM ($p = 0.026$).

Only rectrN produced significantly worse fits to individual histograms when compared to other pdfs. rectrN was significantly worse than RATIO in 10 cases, mixRN in 4 cases, LN in 9 cases, IG in 1 case and GAM in 11 cases. We ranked the goodness of fit of each pdf in the order of the combined $\sum \chi^2 / \sum v$ statistics (summed across all

Table 3 Cumulative goodness of fit test statistics

PDF	$\sum \chi^2$	$\sum v$	$\sum \chi^2 / \sum v$
RATIO	760	393	1.9
LN	1,247	480	2.6
mixRN	938	335	2.8
GAM	1,495	520	2.9
IG	1,503	472	3.2
rectrN	3,680	402	9.2

trials) from smallest to largest (Table 3), and then compared the cumulative goodness of fit of each pdf by performing an F test to check for significant differences between these test statistics. RATIO gave a significantly better fit than LN ($p = 0.002$), mixRN ($p = 0.0002$), GAM ($p = 0.0002$), IG ($p < 0.0001$) and rectrN ($p < 0.0001$). LN did not give a significantly different fit than mixRN ($p = 0.22$) or GAM ($p = 0.14$) but did give a significantly better fit than IG ($p = 0.014$) and rectrN ($p < 0.0001$). MixRN did not give a significantly different fit than GAM ($p = 0.39$) or IG ($p = 0.10$) but did give a significantly better fit than rectrN ($p < 0.0001$). GAM did not give a significantly different fit than IG ($p = 0.12$) but did give a significantly better fit than rectrN ($p < 0.0001$). Finally, IG also gave a significantly better fit than rectrN ($p < 0.0001$).

After correcting for multiple comparisons, there were a number of significant stimulus speed effects on the MLEs of pdf parameters. The value of μ from RATIO increased with increasing stimulus speed ($p < 0.001$), and the correlation between SP amplitude and SP velocity (ρ from RATIO) was significantly lower at a stimulus speed of 10°/s than at higher stimulus speeds ($p < 0.001$). The rate of rise of the diffusion process (μ from IG) decreased with stimulus speed ($p < 0.001$), as did the value μ from LN ($p < 0.001$). The mean estimated percentage of QPs generated by the rogue unit of the mixRN model was 13 % (SD = 12 %). Finally, there were significant between-subjects effects for all of the estimated pdf parameters ($p < 0.002$) indicating that the parameters differ across participants.

Discussion

We have found that the ratio distribution of two correlated and zero-truncated Normal distributions was significantly better (and the reciprocal truncated Normal was significantly worse) at fitting the data than all the other pdfs we have tested. The remaining accumulator models were similar to each other but only moderately successful in their goodness of fit. The statistical tests we have used to compare pdfs have taken into account the number of free parameters estimated for each distribution, and while our

Table 2 Goodness of fit of pdfs to individual histograms

PDF	Histograms that gave a good fit
RATIO	36 (90 %)
mixRN	28 (70 %)
LN	26 (65 %)
IG	25 (63 %)
GAM	23 (58 %)
rectrN	10 (25 %)

proposed ratio distribution has two more free parameters than the other distributions tested (except mixRN, which also has four free parameters), it still performs remarkably well.

We propose that QPIDs are not being determined by one of the ‘interval generator’ mechanisms, but that the brain triggers a QP once eye position reaches a variable amplitude threshold. A similar mechanism has been proposed for generating QPs in vestibular nystagmus where the QP threshold was modelled as a noisy eye position signal (Chun and Robinson 1978), and Lau et al. (1978) have observed that the threshold for triggering a vestibular QP is dependent on both eye position and velocity in humans.

QPID histograms are characteristically positively skewed and appear similar to the distributions described by a number of proposed accumulator models. These models are commonly based on integrate-to-fire models of neuronal activation and have been used to describe the distribution of voluntary saccade latency to stationary targets (Carpenter 1999; Smith and Ratcliff 2004). However, during OKN, the eyes are in a state of continuous motion in the direction of optic flow and it seems likely that the threshold for triggering a QP could depend on eye position—otherwise, the eyes might continue to move until they reach the limit of the orbit. It is well known that there are sources of noise in the motor command signal that generates saccadic eye movements (van Beers 2007), and the end point variance of QPs in OKN would lead to a variable amplitude threshold if the oculomotor system were attempting to maintain some average position of the eyes in the orbit. In agreement with Kolarik et al. (2009), we have found that there is also variability in SP velocity between SPs. As the SPs of OKN are approximately linear, the duration of SPs is plausibly given by the ratio of these two distributed variables.

We found significant correlation between SP amplitude and SP velocity in most trials, in agreement with Watanabe et al. (1994) who used a random dot kinematogram stimulus. It is tempting to speculate that the correlation between SP amplitude and SP velocity reflects a transmission delay or a refractory period during which QPs are not triggered, as a delay in triggering would increase amplitude depending on velocity. The correlation between these two variables and the observation that SPs are only ever made in the direction of stimulus motion means that our proposed ratio distribution should also contain a term to account for the correlation between the quotient variables (which are both only supported in the positive domain). We have assumed that the distribution of SP amplitude and SP velocity would be approximately Normal due to the central limit theorem, but it is possible that other distributions with a strictly positive support could be used to model these variables.

An ‘internal’ model has been proposed to account for voluntary saccade latency that is statistically similar to our ‘external’ model (excluding the correlation term), where a decision signal rises to threshold in a linear manner, but both the rate of rise and the threshold vary from saccade to saccade with a Normal distribution: the extended LATER model (Nakahara et al. 2006). It is difficult to separate the internal model (with a linearly increasing decision signal) from the external model (with a linearly increasing position signal), as the two models are algebraically equivalent for linear SPs. We believe, however, that our model is more parsimonious and also accounts for the correlation between the two quotient variables.

Trillenberget al. (2002) were cautious in their conclusions as the pdfs they tested gave an unsatisfactory fit to the data. We did have a moderate improvement in statistical power as our combined dataset contained 10,280 QP intervals, whereas the largest combined dataset Trillenberget al. tested contained only 5,730 QP intervals. However, our results were predominantly enhanced by including the ratio and mixRN distributions in the analysis, as they provided statistically significant better fits when all datasets were combined.

The MLEs of pdf parameters can give us additional information. We found a significant between-subjects effect for all of the estimated pdf parameters, and a stimulus speed effect for the values of μ and ρ from our ratio distribution. This could explain why we observe such remarkably variable eye movements during OKN, as the form of the distribution may remain the same (a ratio distribution) but the parameters of the distribution depend on stimulus conditions and vary between participants. This requires further investigation but implies that individual differences cannot be ignored in developing a model of OKN.

By collecting large amounts of data, it is possible to distinguish between different models that might otherwise appear similar by eye, and here, we introduce one model that is significantly better than a range of other models at predicting the distribution of QPIDs: a ratio distribution. We propose that QPIDs are determined by the ratio of a variable amplitude threshold and variable SP velocity, with the additional constraint that SPs have approximately linear trajectories.

Acknowledgments This research was supported by an Engineering and Physical Sciences Research Council Standard Research Student award (DTG: EP/P502675/1).

Appendix: Derivation of the pdf of the ratio of two correlated truncated Normal variables

The pdf of the ratio of two Normal random variables, x and y , is given by:

$$z = x/y. \quad (3)$$

From basic probability theory, the pdf of z is given by:

$$f_z(z) = \int_{-\infty}^{\infty} |y| f_{xy}(yz, y) dy \quad (4)$$

where $f(x, y)$ is the bivariate Normal pdf. If x and y are left truncated at zero, then the pdf of z becomes:

$$f_z(z) = \int_0^{\infty} y f_{xy}(yz, y) dy. \quad (5)$$

The bivariate Normal pdf, $f(x, y)$, is given by the normalised two-dimensional Gaussian, $G(x, y)$:

$$f(x, y) = \frac{1}{k} G(x, y) \quad (6)$$

where:

$$G(x, y) = \exp\left(-\frac{1}{2(1-\rho^2)}\left[\frac{(x-\mu_x)^2}{\sigma_x^2} + \frac{(y-\mu_y)^2}{\sigma_y^2} - \frac{2\rho(x-\mu_x)(y-\mu_y)}{\sigma_x\sigma_y}\right]\right), \quad (7)$$

k is a normalising constant such that the area under $G(x, y)$ is unity for the quadrants considered, $\rho = \sigma_{xy}^2 / \sigma_x \sigma_y$ is the correlation coefficient of x and y , and σ_{xy}^2 is the covariance. For all quadrants:

$$k = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} G(x, y) dx dy = 2\pi\sigma_x\sigma_y\sqrt{1-\rho^2}. \quad (8)$$

For the ratio of truncated Normals

$$k_1 = \int_0^{\infty} \int_0^{\infty} G(x, y) dx dy \quad (9)$$

and is found numerically.

We can expand the Gaussian in eq. 7 in the form:

$$G(yz, y) = \exp(ay^2 + by + c) \quad (10)$$

where:

$$a = \frac{-(z^2\sigma^2 - 2z\rho\sigma + 1)}{2\sigma_y^2(1-\rho^2)} < 0, \quad (11)$$

$$b = \frac{\mu_x(z\sigma^2 + \mu - z\rho\sigma\mu - \rho\sigma)}{\sigma_y^2(1-\rho^2)}, \quad (12)$$

$$c = \frac{-\alpha(\sigma^2 - 2\rho\mu\sigma + \mu^2)}{2(1-\rho^2)}, \quad (13)$$

$$\mu = \mu_y/\mu_x, \sigma = \sigma_y/\sigma_x \text{ and } \alpha = \mu_x^2/\sigma_y^2.$$

Now consider the integral:

$$f_z(z) = \frac{1}{k_1} \int_0^{\infty} y G(yz, y) dy = \frac{1}{k_1} \int_0^{\infty} y \exp(ay^2 + by + c) dy. \quad (14)$$

With integration by parts:

$$f_z(z) = -\frac{\exp(c)}{2ak_1} \left(1 + b \int_0^{\infty} \exp(ay^2 + by) dy\right). \quad (15)$$

Substituting $u = y\sqrt{-a} - b/2\sqrt{-a}$ and $d = b/\sqrt{-a}$, we have:

$$f_z(z) = -\frac{\exp(c)}{2ak_1} \left[1 + \frac{d\sqrt{\pi}}{2} \exp\left(\frac{d^2}{4}\right) \operatorname{erfc}\left(-\frac{d}{2}\right)\right] \quad (16)$$

where:

$$d = \frac{\sqrt{2\alpha}(z\sigma^2 + \mu - z\rho\sigma\mu - \rho\sigma)}{\sqrt{(1-\rho^2)}(z^2\sigma^2 - 2z\rho\sigma + 1)} \quad (17)$$

Thus, the pdf of the ratio of two correlated and truncated Normal variables can be described with just four parameters:

$$\mu = \frac{\mu_y}{\mu_x}, \sigma = \frac{\sigma_y}{\sigma_x}, \alpha = \frac{\mu_x^2}{\sigma_y^2}, \text{ and } \rho.$$

References

- Anastasio TJ (1996) A random walk model of fast-phase timing during optokinetic nystagmus. *Biol Cybern* 75:1–9
- Balaban CD, Ariel M (1991) A “beat-to-beat” interval generator for optokinetic nystagmus. *Biol Cybern* 66:203–216
- Carpenter RHS (1993) Distribution of quick-phase intervals in optokinetic nystagmus. *Ophthalmic Res* 25:91–93
- Carpenter RHS (1994) Express optokinetic nystagmus. In: Fuchs AF, Brandt T, Büttner U, Zee D (eds) *Contemporary ocular motor and vestibular research*. Georg Thieme, Stuttgart, pp 185–187
- Carpenter RHS (1999) Visual selection: neurons that make up their minds. *Curr Biol* 9:595–598
- Carpenter RHS, Williams ML (1995) Neural computation of log likelihood in control of saccadic eye movements. *Nature* 377: 59–62
- Chun KS, Robinson DA (1978) A model of quick phase generation in the vestibuloocular reflex. *Biol Cybern* 28:209–221
- Harris CM, Waddington J (2012) On the convergence of time interval moments: caveat sciscitator. *J Neurosci Methods* 205:345–356
- Holm S (1979) A simple sequentially rejective multiple test procedure. *Scand J Stat* 6:65–70
- Kolarik AJ, Margrain TH, Freeman TCA (2009) Precision and accuracy of ocular following: influence of age and type of eye movement. *Exp Brain Res* 201:271–282
- Lau CGY, Honrubia V, Baloh RW (1978) The pattern of eye movement trajectories during physiological nystagmus in humans. In: Hood JD (ed) *Vestibular mechanisms in health and disease*. Academic, New York, pp 37–44
- Nakahara H, Nakamura K, Hikosaka O (2006) Extended LATER model can account for trial-by-trial variability of both pre- and post-processes. *Neural Netw* 19:1027–1046

- Smith PL, Ratcliff R (2004) Psychology and neurobiology of simple decisions. *Trends Neurosci* 27:161–168
- Trillenber P, Zee DS, Shelhamer M (2002) On the distribution of fast-phase intervals in optokinetic and vestibular nystagmus. *Biol Cybern* 87:68–78
- Tuckwell H (1988) *Introduction to theoretical neurobiology: nonlinear and stochastic theories*. Cambridge University Press, Cambridge
- van Beers RJ (2007) The sources of variability in saccadic eye movements. *J Neurosci* 27:8757–8770
- Watanabe Y, Ohmura A, Shojaku H, Mizukoshi K (1994) Optokinetic nystagmus elicited by a random dot pattern and a wide interval stripe pattern in normal subjects. *Acta Otolaryngol Stockh* 511:104–108